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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,494	03/23/2004	Mark G. Resnick	SOM700/4-009(A)8CON2/6400	2768

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EXAMINER
CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 09/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/806,494	RESNICK, MARK G.	
	Examiner	Art Unit	
	Lakshmi S Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 31-53 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 31-53 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3-23-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-30 have been canceled. Claims 31-53 are presented for examination.

Claim Rejections - 35 USC § 112

Claims 31-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing photodamage to skin cells, does not reasonably provide enablement for preventing photodamage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: nature of the invention, breadth of the claims, state of the art, guidance of the specification, predictability if the art, and the working examples. All the factors have been considered with regard to the claim, with the most relevant factors discussed below.

Nature of the Invention and Breadth of Claims: All rejected claims are drawn to the methods of preventing or reducing photodamaged to the skin cells of a subject comprising administering instant composition comprising selegiline and/or desmethylselegiline in an amount to reduce apoptosis of skin cells exposed to electromagnetic or ionizing radiation. The nature of the invention is extremely complex in that it encompasses anticipating multiple complex symptoms, diseases, conditions or disorders caused to due to photodamage and subsequently administering the instant composition. The breadth of the claims exacerbates the complex nature of the claims. Moreover, the specification describes that photodamage caused by exposure to electromagnetic radiation in the UV and visible light and ionizing radiation results in the development of non-melanoma skin cancer, immune function suppression and photoaging. Thus,

the term "preventing" in the instant claims encompasses a broad range of conditions and associated diseases/disorders under the umbrella of photoaging, non-melanoma skin cancer and immune function suppression.

State of the Art and Guidance of the Specification: The state of the art does not recognize the administration of compositions to prevent the photodamage as required in the instant claims. The state of the art recognizes the treatment of the symptoms of these disorders but not their cure. The guidance given by the specification on how to prevent the disorders is absent. Applicants state that the compounds promote healing of photodamaged skin as evidenced by a reduction in one or more symptoms i.e., edema, vasodilation, lymphocyte infiltration, spongiosis of epidermis etc. Further, in the examples the effect of claimed compounds in reducing apoptosis of keratinocytes exposed to UVB radiation. However, prevention or reduction of apoptosis in conditions like melanoma and other skin cancers, which are characterized by uncontrolled cell growth, does not result in reduced photodamage. In fact, the literature on this aspect proves that an anti-apoptotic compound does not necessarily is anti-cancerous. In other words, reducing apoptosis under such conditions would only increase the growth of cancerous cells and not the opposite. (See attached US patent No. 6465440 to von Borstel et al, col. 2, lines 14-49). Von Borstel et al clearly state that agents, which promote cell survival (e.g. by inhibiting apoptosis) after irradiation are not necessarily anti-carcinogenic, and may actually enhance mutation frequency and risk of malignant transformation by permitting survival of damaged cells that would otherwise be eliminated by apoptosis. Thus, the apoptosis reduction in the instant examples does not prevent the photodamaged or reduce skin in melanoma. Further, in view of the teachings of von Borstel et al, i.e., reducing apoptosis is not

favorable in cancerous cells, without sufficient guidance or teaching one of an ordinary skill in the art would not be able to practice the instant invention in melanoma cells and also would not be able to determine as to how to prevent or promote healing in melanoma cells using instant compounds and what markers to use to determine for such treatment. Besides, non-melanoma skin cancer, instant claims also recite immune system dysfunction, which is very broad in terms of the conditions and diseases with the term. While immune system dysfuntion can result in numerous diseases or disorders known to-date, the tem encompasses those that are yet to be identified. The specification lacks any guidance to how to prevent any of these unknown or unidentified conditions by administering instant compositions. Applicants have not provided any guidance to know if all kinds of ionizing and electromagnetic radiation result in the same kinds of photodamaged conditions in all the subjects.

The lack of significant guidance from the specification or prior art with regard to completely controlling or preventing the claimed conditions of skin with the administration of the instant composition makes practicing the claimed invention unpredictable in terms of the prevention of the disease.

The Amount of Experimentation Necessary: In order to be able to prevent photodamage a skilled artisan would have to know the specific conditions being prevented, the intensity of skin damage and associated conditions resulting from the damage due to exposure to ionizing and electromagnetic radiation, length of treatment, end points to look for in order to ensure complete prevention. Instant application has not provided any guidance in this regard. Therefore, the practitioner would turn to trial and error experimentation to use the instant compositions for preventing or reducing photodamaged to the skin cells of a subject so as to

reduce apoptosis of skin cells exposed to electromagnetic or ionizing radiation. Therefore, undue experimentation becomes the burden of the practitioner.

For examination purposes, the phrase "preventing" is interpreted as "treating" the instant conditions.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 31-53 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,709,664. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant method of preventing or reducing or treating photodamage encompasses the patented method of treating wounds and burns. This is also supported by applicants' own admission that ionizing radiation, in photodamage, includes edema, neutrophilic infiltration in dermis, edema etc., all of which are also seen in wounds and burns. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the composition of 6,461,619, for treating wounds, to successfully treat the same underlying conditions in

photodamaged skin.

Claims 31-53 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,461,619. Although the conflicting claims are not identical, they are not patentably distinct from each other because both instant application and patent claims method of preventing or reducing or treating photodamage by administering an effective amount of selegiline or desmethyl selegiline (DMS), as described in patented claims. This is also supported by applicants' own admission that ionizing radiation, in photodamage, includes edema, neutrophilic infiltration in dermis, edema etc., all of which are also encompassed by instant "photodamage" conditions. Further, instant limitation "in an amount to reduce apoptosis" includes the same amount of active agents (see instant dependent claims 34 and 45) is the same as the amount of selegiline and DMS of the patent. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to use the composition of 6,461,619, for treating wounds, to successfully treat the same underlying conditions in photodamaged skin. Thus, the patented claims anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tatton et al (Neurology, 1996) in view of US 5,744,499 to Quash et al (hereafter Quash) OR Quash in view of Tatton et al OR unpatentable over US 5,783,606 to Tatton (Tatton '606) in view of Quash and Tatton et al.

Tatton et al teach deprenyl (same as selegiline) for reducing neuronal apoptosis caused by oxidative free radical damage and the reduction is mediated by a principal metabolite of deprenyl, desmethyldeprenyl (same as desmethylselegiline). Tatton does not teach treating a subject for photodamage skin. Tatton also fails to teach a specific enantiomer of selegiline or desmethylselegiline.

Quash teaches modulation of apoptosis (induce or suppress) as a mechanism to prevent or provide treatment for photoinduced or chronological aging of skin and other related skin conditions. Quash suggests aging of skin involves apoptosis (col. 2, lines 6-10) and suggests compounds modulating apoptosis for preventing the appearance or signs of aging such as wrinkles. Quash also teaches that under some conditions apoptosis needs to be induced and in others apoptosis is inhibited and teaches dermatological conditions such as keratinization disorders including keratoderma, icthyosis, acne, psoriasis, eczema, epidermal or dermal hyperproliferation (col. 6 through col.7). Quash teaches the composition containing apoptosis inducer or a suppressor, in the form of a cream, patch, lotion, gel etc (col. 8) and teaches adding several additives such as moisturizes, pH regulators (col. 9). Quash does not teach selegiline or dimethyl selegiline.

Tatton '606 teaches deprenyl and desmethyldeprenyl compounds for the treatment of glaucoma (col. 3, lines 56-63). Tatton '606teaches administering deprenyl compositions in the form of sprays, liquids, gels, pastes etc., for oral, nasal, topical or other routes (col. 12).

It would have been obvious for one of an ordinary skill in the art the time of the instant invention to use the anti-apoptotic compounds (deprenyl and desmethyldeprenyl) of Tatton et al (Neurology) for inhibiting or suppressing apoptosis in several dermal or epidermal conditions such as aging because Quash teaches that skin aging basically result from malfunctioning of skin mechanisms, especially due to apoptosis and suggests any species capable of modulating apoptosis can also prevent aging and its signs such as wrinkles. Therefore, one of an ordinary skill in the art would have expected the compounds of Tatton et al to be effective in reducing or suppressing apoptosis in conditions which require modulating apoptosis i.e., psoriasis, inflammation, keratoses, dermal or epidermal hyperproliferation (as taught by Quash). Similarly, one of an ordinary skill in the art would have incorporated the compounds of Tatton et al in the composition Quash and use for treating and/or combating photoinduced or chronologic aging of the skin by modulating apoptosis because Tatton et al suggests that the claimed compounds have the ability to reduce oxidative free radical initiated apoptosis.

Alternatively, it would have been obvious for one of an ordinary skill in the art the time of the instant invention to use selegiline or desmethylselegiline of Tatton '606 for providing or combating aging in skin by inhibiting apoptosis because Quash teaches inhibiting apoptosis provides a treatment to aging skin and Tatton et al teaches that deprenyl and desmethyldeprenyl are effective anti-apoptotic agents which reduce apoptosis caused by oxidative free radicals. Further, formulation the anti-apoptotic compositions containing deprenyl or desmethyldeprenyl,

their appropriate or suitable enantiomers for effective inhibition of apoptosis, preparing the composition in the form of a spray, cream, patch etc., containing the optimum amount of the effective compound with an expectation to achieve an apoptotic effect would have been within the scope of a skilled artisan. Examiner notes that instant claim 43 recite treating a subject "for treating photodamage" where treating for photodamage is not a positive limitation. Instead, it is suggested to amend the claim to recite "A method of treating photodamaged skin in a subject".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 7.30 AM -4.00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615
September 26, 2004